



PATENT

09/218,481

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: VAN BRUGGEN ET AL. Examiner: J. HUNT
Serial No.: 09/218,481 Group Art Unit: 1642 *H*
Filed: DECEMBER 22, 1998 Docket No.: 11669.113US01 *24/15*
Title: VASCULAR ENDOTHELIAL CELL GROWTH FACTOR
ANTAGONISTS AND USES THEREOF *1/17/03*

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AMENDMENT AND RESPONSE

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Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In response to the Office Action mailed June 25, 2002, Applicants request entry of the following amendment and consideration of the following remarks.

In the Specification

Please replace the paragraph beginning at page 13, line 11, with the following rewritten paragraph.

Particular humanized antibodies contemplated for use in the present invention include the humanized and affinity matured anti-hVEGF antibodies described in published PCT application WO 98/45331 (published October 15, 1998) and WO 98/45332 (published October 15, 1998). *C1*

Such humanized or affinity matured anti-VEGF antibodies may be prepared or made using the methods and techniques described in WO 98/45331 and WO 98/45332. Preferably, the anti-hVEGF antibody comprises the humanized F(ab), designated F(ab)-12, or the affinity matured antibody, designated as YO317, in the above referenced PCT applications. Figures 14-A and

E1
15A-B illustrate the amino acid sequences (light and heavy chains) for these anti-VEGF antibodies, along with other affinity matured anti-VEGF antibodies, designated as YO192; YO238-3; YO239-19; YO313-2; YO234-1; and YO313-1. All such anti-VEGF antibodies are contemplated for use in the methods described herein. As disclosed in these published PCT applications, several of the humanized and affinity matured antibodies were demonstrated to reduce or inhibit the activity in different types of *in vitro* assays, and thus act as VEGF antagonists.

In the Claims

Please amend claim 1 as follows:

E2
1. (Amended) A method of reducing cerebral edema mediated by VEGF in a mammal, comprising administering to said mammal a hVEGF antagonist in an amount effective to reduce the volume of cerebral edema in the brain of said mammal, wherein said hVEGF antagonist comprises an anti-hVEGF antibody.